RUNX1 in maintenance, expansion, and differentiation of therapeutic pluripotent stem cells

Grant Award Details

RUNX1 in maintenance, expansion, and differentiation of therapeutic pluripotent stem cells

Grant Type: Basic Biology II

Grant Number: RB2-01645

Project Objective: The goal of this project is to test the hypothesis that two different isoforms of RUNX1 play differing roles in regulating hematopoiesis from hESC and hiPSC, and that their manipulation might lead to improved methods for isolating therapeutic populations of HSC from human pluripotent stem cells

Investigator:

Name:	Dong-Er Zhang
Institution:	University of California, San Diego
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Award Value: $1,371,540

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3 + NCE (new period 8/2/12 - 10/31/13)

View Report

Grant Application Details

Application Title: RUNX1 in maintenance, expansion, and differentiation of therapeutic pluripotent stem cells

Public Abstract: Recent technical advancements in human embryonic stem cell (ESC) and induced pluripotent stem cell (iPSC) production have revolutionized their potential applications in regenerative medicine. However, a remaining big hurdle in this process is the need for efficient, effective, and stable generation of specific cell types from such stem cells for therapeutic usage. The ultimate goal of the proposed study is to identify approaches to increase the production of therapeutically useful blood cells from human ESCs and patient-specific iPSCs. Currently, bone marrow transplantation is the best way to cure many blood-related disorders, such as sickle cell anemia, thalassemia, and blood cancers like leukemia. Furthermore, blood transfusion is an effective way to rapidly counteract blood cell loss due to ablative treatments, such as chemotherapy and radiation therapy. Unfortunately, the limiting factor in transplantation and transfusion treatments is the lack of matched donors. The ability to producing unlimited numbers of blood stem cells and/or functioning differentiated blood cells from human ESCs and patient-derived iPSCs will greatly improve the opportunity of such treatments.

In this application, we propose experiments to examine how specific factors that control gene expression can promote blood cell formation, expansion, and differentiation from human ESCs and iPSCs. We plan to use experimental tools to control the time and amount of expression of these factors in human ESCs and iPSCs during their growth in the tissue culture. Furthermore, we will study the generation of blood cells based on specific markers present on the blood cell surface. Current technology used to produce iPSCs utilizes retroviruses to introduce genetic material. To avoid the creation of unfavorable mutations due to random insertion of DNA fragments into the genomes of these cells, we will also explore the possibility of delivering cell membrane penetrating versions of these factors in cell culture medium.

The proposed studies will provide valuable insight into the control of stem cell differentiation and the therapeutic usage of factors that regulate gene expression, which are highly relevant to the main goals of CIRM.

Statement of Benefit to California: Thousands of Californians are suffering from blood-related diseases that may potentially be cured with bone marrow transplantation and/or blood transfusion. However, these life-saving measures are limited by a lack of eligible donors and the necessity of finding correctly matched blood products. Current treatments for some of these conditions can cost patients tens of thousands of dollars per year. Despite these treatments, many patients die from their disease waiting for a bone marrow transplant. Recent technical advancements in human embryonic stem cell (ESC) and induced pluripotent stem cell (iPSC) production have revolutionized their potential applications in regenerative medicine and have provided enormous hope for these patients. Based on our accumulated knowledge in blood cell-related research, we propose to identify useful tools and methods to enhance the specificity and efficiency in the production of blood cells from human ESCs and iPSCs. Producing therapeutically useful differentiated cells from pluripotent stem cells is a critical step in raising ESCs and iPSCs into the realm of clinical application. Therefore, one long term benefit of the proposed work is to improve the treatment of thousands of Californian patients who need to receive healthy, functioning blood cells to alleviate their disease conditions. In turn, this will benefit California's financial status in reducing the cost of treating these patients with expensive yet ineffective methods.

The proposed research will continue to maintain California's leadership in the field of stem cell research. Our proposal will provide a better understanding of the mechanisms involved in producing blood stem cells and mature blood cells from ESCs and iPSCs. We will also explore the use of a novel method in producing these cells, and thus enhance the field of stem cell biology. In addition, the involved work will include the training and education of some of California's bright young minds. This preparation will instill in them an enthusiasm for biomedical research and allow them to become successful scientists in the future.

Source URL: https://www.cirm.ca.gov/our-progress/awards/runx1-maintenance-expansion-and-differentiation-therapeutic-pluripotent-stem